REMARKS

A further clerical error was detected on page 21 of the specification, and the paragraph beginning at line 11 has been corrected. It is believed that it is quite clear from the preceding paragraph that it is the I-ratios, not the N-ratios, that are adjusted to obtain the A-ratios.

It is submitted that independent claims 1, 20 and new claim 22 would not be obvious from the disclosure of published U.S. Application 2003/0054386 to Antonarakis et al. (hereinafter Antonarakis et al.) in view of the disclosure of U.S. Patent No. 6,251,601 to Bao et al. (hereinafter Bao et al.). Antonarakis et al. have located paralogous nucleic acid sequences on different chromosomes which have greater than 80% identity and are of substantially the same length so that they can be amplified through PCR using a single pair of primers. The use of a single pair of primers is stressed throughout the disclosure in paragraphs 15, 16, 17, 25, 26, 27, 28, 93 and 116, for example. Whereas this might well produce a quantitative result, it is limited to analyzing for one specific chromosomal abnormality at a time.

As indicated in the first two lines of each of Applicant's independent claims, a method is provided for detecting any one of multiple chromosomal disorders in a single assay. In contrast to Antonarakis et al., Applicant employs different sets of primers which include pairs that are targeted to different selected segments of different chromosomes and one pair that is targeted for a single segment of a single control gene. It is submitted that amended claims 1 and 20 and new claim 22 not only recite the use of pairs complementary to the sense and antisense strands of each targeted sequence, but use different pairs targeted to multiple sequences and to one particular reference/control gene.

With respect to the Bao et al. disclosure, the use of PCR is only mentioned as a preliminary step in obtaining one of the three nucleic acid populations to be used in the assay. It is mentioned that if there is insufficient cDNA available, such can be amplified by PCR to provide one starting material which is then labeled with fluorescent markers of one color. PCR is not a part of the assay procedure. As pointed out in column 3, the Bao et al. intention is to use CGH and a microarray for simultaneously hybridizing to three

separate populations: a cDNA population having a first fluorescent color, a chrosomosomal DNA population having a second fluorescent color, and a reference nucleic acid population labeled with a third fluorescent color. Following hybridization with the microarray, each of the spots will have adhered thereto labeled nucleic acids from all three of the populations. The algorithm which is employed is simply one to adjust the results for the purpose of minimizing local background. The adjustment of intensities set forth in the paragraph in column 18 to which attention was called is clearly to correct for background difficulties in using three different-colored fluorescent labels at each microspot on the array.

In summary, Bao et al. are running simultaneous hybridization assays with three different populations. They are not, as specified in claim 1, comparing the imaging of relevant spots on the microarray for each targeted sequence to that of a single control gene, and then to results obtained from similar testing of multiple samples of genomic DNA known to be normal. The recitation in claim 20 that the N-ratios are averages for normal DNA of persons is, of course, also an expression of the use of such multiple normal samples for reference. New claim 22 recites in detail the diagnosis; it points out that the I-ratios are adjusted to A-ratios by dividing by the average C-factor that is obtained in the manner recited with respect to all of the C-factors within a specified range obtained from the imaging of the different microspots on the microarray. Such would not be obvious from the Bao et al. disclosure.

Thus, it is requested that the rejection on the basis of the combination of these two references be reconsidered and withdrawn. It is submitted that these three independent claims should be allowed.

The secondary references to Fulcrand et al. and Lockhart et al. were applied only with respect to certain of the dependent claims. They are addressed to the specific use of certain primers and digestion with an exonuclease, as well as the selection of GAPD as a control gene, but they do not otherwise supply a teaching of any of the deficiencies mentioned above.

In view of the foregoing, it is submitted that, in the absence of any more pertinent prior art, independent claims, 1, 20 and 22, and the claims dependent thereupon, namely claims 2-11 and 21 should be allowed, and allowance thereof is respectfully requested. Favorable action is accordingly courteously solicited.

Respectfully submitted,

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